

**Remarks**

1. – 6, and 8.      Restriction/Election: The Applicants affirm the election to prosecute the invention of Group I, Claims 1-5 and 30-31. Consistent with the election, Claims 6-29 and 32-59, being withdrawn from further consideration, are hereby cancelled.

7.      Applicants note the reminder regarding inventorship and its relationship to claim cancellation and affirm that the correct inventors are named in this case.

9.      Drawings: The Applicants note the Draftsman's approval of the drawing.

10.     Oath/Declaration      A new oath/declaration by the newly added inventor 'Edward J. Whittle' is being prepared for submission.

11.     Specification: The Applicants have reviewed the specification and have amended the specification as noted on pages 2-5 of this paper. The amendment of the specification contains no new matter.

12.     Rejection under 35 U.S.C. §102

In making this rejection of the claims under consideration in this case, the Examiner cites three publications:

1.      Cahoon et al. [PNAS 94:4872-4877, May 1997];
2.      US Patent 5,705,391 (Cahoon et al., Jan 6, 1998); and

3. US Patent 5,888,790 (Cahoon et al., March 30, 1999 – filed May 9, 1997)

The Examiner states that reference 1 (“entire document, especially abstract, Fig. 3, and page 4875-column 2) “teaches castor mutants or modified  $\Delta^9$ -18:0-ACP desaturase” and that “characterization of specific mutants at positions 114, 117, 118, 179, 181 & 188 are also taught” and thus the reference “anticipates the claims”.

The Examiner states that the inventors of reference 2 “teach mutant or modified  $\Delta^9$ -18:0-ACP desaturase (see column 4, last paragraph) at the identified contact residues M114, L115, T117, L118, G188, & F189” and therefore the reference anticipates the claims.

The Examiner further states that the inventors of reference 3 “teach mutant or modified  $\Delta^9$ -18:0-ACP desaturase (see claims 10-12) at the identified contact residues M114, L115, T117, L118, G188, & F189.” Further stating that “the claims are drawn to any amino acid substitution at the positions indicated and encompass the specific amino acid substitution(s) claimed” therefore the reference anticipates the claims. (*emphasis added*).

In view of the Amendment of the Claims in this paper, pages 6-7, the Applicants respectfully request the reconsideration and withdrawal of this basis for rejection of the claims for the following reasons.

Reference 1 (Table 1), Reference 2 (Figure 1) and Reference 3 (Table 1 and Figure 1) teach two different replacements of 5 or 6 amino acids in the *T. alata*  $\Delta^6$ -16:0-ACP desaturase with cognate amino acids from the castor  $\Delta^9$ -18:0-ACP desaturase so as to increase the  $\Delta^6$ -16:0 enzyme’s activity with longer, i.e. 18 carbon atom, substrates, as follows

(where numbering of amino acid positions refers to the mature  $\Delta^9$ -18:0 desaturase of *T. alata*):

Construct 1: A181T; A200F; S205N; L206T; G207A

Construct 2: A181T; A188G; Y189F; S205N; L206T; G207A

The references also teach two double replacements in the  $\Delta^6$ -16:0 enzyme as follows:

Double 1: A188G; Y189F      Double 2: A181T; A200F

None of the mutated *T. alata* 16:0 desaturases suggest the mutant 18:0 desaturases of the present invention. Thus, this aspect of References 1 and 2 cannot anticipate the claims of the present invention.

With respect to modifying the castor  $\Delta^9$ -18:0-ACP desaturase, References 2 and 3 state that "preliminary experimental work has revealed that a single amino acid substitution at position 118 (Leu to Phe) in castor  $\Delta^9$  acyl-ACP desaturase results in an approximately 10-fold increase in its activity with 16:0-ACP" (Reference 2: column 4 lines 66-67, column 5 lines 1-2; Reference 3: column 5, lines 9-13). This single replacement is not claimed in the present invention, either in the claims as filed or in the claims as amended herein. Thus this aspect of References 2 and 3 cannot anticipate the claims.

In addition, References 1 and 3 specifically teach a double mutant in which Leu 118 is replaced with Phe and Pro 179 is replaced with Ile in the castor  $\Delta^9$ -18:0-ACP desaturase to cause its activity to increase with 16:0 fatty acids (see Fig. 3, and page 4875 column 2 and page 4876, column 1 of Reference 1). Neither of these replacements are claimed in the

present invention, neither in the originally filed claims or in the claims as amended in this paper. Therefore this aspect of References 1 and 3 cannot anticipate the claims.

Furthermore, References 1 and 3 do not in any way suggest nor do they provide guidance as to how to arrive specifically at any of the substitutions of the present invention.

The Examiner accurately states that Claim 10 of Reference 3 is drawn to a mutant acyl-ACP desaturase having an amino acid substitution at a contact residue within the substrate binding channel. Claims 11 and 12, depending therefrom, suggest that the residue to be substituted be selected from among eight residues: 114, 115, 117, 118, 179, 181, 188 and 189. However because there is no guidance in the cited references (other than the aforementioned single and double mutants of the castor 18:0 desaturase), there are 19 (different amino acids) X 8 (positions to be substituted) = 152 choices of single amino acid substitutions that could be made in order to practice the invention of Claims 10-12 of Reference 3. One of skill in the art could make all 152 possible single substitutions, but would also readily recognize the likelihood that few of the 152 possible mutants would have the requisite altered activity. With the exception of the suggestions in References 1, 2 and 3 to replace either only Leu 118 with Phe or to replace both Leu 118 with Phe and Pro 179 with Ile, there is no guidance in References 1, 2 or 3 that would give one of skill in the art a reasonable expectation of success of practicing Claims 10-12. An undue amount of experimentation would be required in order to arrive at the functional mutant desaturases claimed in the present invention. The claims of the present invention, as herein amended, are

clearly distinct from the prior art of Reference 1 and the inventions claimed in References 2 and 3.

The claims of the present invention, as herein amended, pages 6-7 of this paper, are drawn to mutant castor  $\Delta^9$ -18:0-ACP desaturases having increased activity towards fatty acids having fewer than 18 carbon atoms, said mutant having two or more specifically identified amino acid substitutions. The specification of the present invention provides one of skill in the art with all of the necessary guidance to practice the invention as claimed.

Thus, while the cited references 1, 2 and 3 identify amino acid residues 114, 115, 117, 118, 179, 181, 188 and 189 of the castor  $\Delta^9$ -18:0-ACP desaturase as being involved in substrate chain length and regio- specificity, the references provide no guidance (other than replacement of Leu 118 with Phe and Pro 179 with Ile) as to how or whether to replace one or all of those eight amino acids in order to increase the activity with fatty acids having fewer than 18 carbon atoms. There are  $20^8$  ( $2.56 \times 10^9$ ) possible combinations of all 20 amino acids in those eight positions. On this basis alone, in the absence of any further guidance, these references certainly cannot anticipate the claims of the present invention.

In light of the above, the Applicants' Agent asked the inventors to review the references in depth to determine what guidance (other than L118F or L118F/P179I) may be provided in the cited references as to which modifications or substitutions might cause the mutant 18:0 desaturase to have an increased activity with fatty acid substrates having fewer

that 18 carbon atoms. This review is contained in the inventor's Declaration under C.F.R. §1.132, attached to this paper.

The conclusion reached by the inventors is that the guidance provided in the references would not create a reasonable expectation of success in achieving a goal of creating any of the mutant  $\Delta^9$ -18:0-ACP desaturases claimed in the present invention. The guidance of the cited Reference is unlikely to specifically, and without undue experimentation, guide one of skill in the art to produce any of the specific mutant desaturases of the present invention.

The inventors point out that of the over 800 possible mutants suggested in the reference only one double mutant could be construed as being suggested by the guidance they have found. However, one would be required to prepare 61 double mutants to discover the double mutant suggested in Reference 1, Figure 4 (*i.e.*, the double mutant of Claim 3 as herein amended). Because this double mutant is only one of 61 potential choices for double mutants suggested by the information of Figure 4, Figure 4 of Reference 1 provides insufficient guidance to one of skill in the art to arrive at the mutants of the present invention without undue experimentation and therefore cannot anticipate the claims.

#### 15. Double Patenting:

The Examiner indicates that the claims of the present invention are rejected under the judicially created doctrine of double patenting over Claims 10-12 of Reference 3, US Patent 5,888,790, which was also cited in the rejection under 35 USC §102.

The Applicants respectfully request reconsideration and the withdrawal of this basis for rejection of the Claims, as herein amended, as the Claims of the present case are clearly drawn to an invention that is neither contemplated nor suggested by the cited Claims. Furthermore, as discussed above, there is no guidance provided in US Patent 5,888,790 that would give one of skill in the art a reasonable expectation of success in creating the mutant 18:0 desaturases of the present invention.

16. Provisional Double Patenting Rejection.

The Examiner indicates that the Claims in the case are provisionally rejected under the doctrine of double patenting over Claims 28-42 of the co-pending Application No. 09/988,929.

The Applicants respectfully request withdrawal of this basis of rejection of the Claims of the present application. The cited claims 28-42 of the co-pending case have been withdrawn from consideration and cancelled as being drawn to a non-elected invention. Should the Claims in the present case be allowed, it is unlikely that the Applicants would seek allowance of the cited claims in a Divisional application of the co-pending case.

Additional Remarks

Cancellation of Claims:

Claims 2, 30 and 31 have been cancelled.

Claims 6-29 and 32-59 have been withdrawn and cancelled (page 8 of this paper).

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Amendments of the Claims:

Claims 1, 3, 4 and 5 have been amended to more particularly point out and distinctly claim the mutant desaturases of the present invention. The amended Claims contain no new matter.

New Claim 60 has been added. Claim 60 contains no new matter.

In light of the above Amendments and Remarks, applicants respectfully submit that the instant application is now in condition for allowance and solicit a timely notice of allowance.

Respectfully submitted,



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